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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/039,171 | 01/03/2002 | Robert Haley | UTSD:749US | 7156 |
| 7590 Steven L. Highlander FULBRIGHT & JAWORSKI L.L.P. 600 Congress Avenue Suite 2400 Austin, TX 78701 | | 12/22/2006 | EXAMINER WHITEMAN, BRIAN A | |
| | | | ART UNIT 1635 | PAPER NUMBER |
| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE | | |
| 3 MONTHS | 12/22/2006 | PAPER | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/039,171 | HALEY ET AL. | |
| | Examiner | Art Unit | |
| | Brian Whiteman | 1635 | |

— The MAILING DATE of this communication appears on the cover sheet with the correspondence address —
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 17 November 2006.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-5 and 9-25 is/are pending in the application.
 - 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-5,9-25 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____. | 5) <input type="checkbox"/> Notice of Informal Patent Application 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

Claims 1-5 and 9-25 are pending.

Applicant's argument filed on 11/17/06 is acknowledged and considered by the examiner.

The finality of the rejection of the last Office action is withdrawn in view of applicant's argument that at the time of filing gene therapy was considered enabled and the new rejections set forth below.

Instant claims 1-5 and 9-20 read on a method of delivering an expression cassette comprising a promoter operably linked to a gene encoding PON1 to a cell either in vitro or in vivo, wherein said expression cassettes expresses PON1 in said cell resulting in detoxification of said organophosphate toxin when the cell is exposed to the toxin.

Election/Restrictions

Claim 2 and 22 are rejoined with the elected invention and examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 and 9-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of protecting a cell from organophosphate toxin comprising administering an expression cassette comprising a CMV promoter operably linked to a PON1 gene and exposing the cell to the organophosphate toxin, wherein expression of the

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PON1 gene results in detoxification of said organophosphate toxin, does not reasonably provide enablement for using a genus of promoters to express the PON1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosure in the application coupled with information known in the art without undue experimentation (*United States v. Teletronics, Inc.* 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based upon a single factor, but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In Re Wands* as set forth above.

Instant claims 1-5 and 9-20 read on a method of delivering an expression cassette comprising a promoter operably linked to a gene encoding PON1 to a cell either in vitro or in vivo, wherein said expression cassettes expresses PON1 in said cell resulting in detoxification of said organophosphate toxin when the cell is exposed to the toxin.

Applicants teach the use of recombinant adenovirus comprising a CMV operably linked to a gene encoding either PON1 type R or type Q followed by chlorphyrifos challenge in mice (pages 43-44). The mice receiving the adenovirus were protected or partially protected from chlorphyrifos. However, the art of record teaches that although the generating mouse lines that express human PON1 using human cDNA constructs were not successful (Furlong et al., *supra*).

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Furlong futher teaches that, "Since the regulatory mechanism of human PON1 expression has not yet been identified, it is unknown whether any cis-acting elements required for PON1 transcription are included in these constructs (page 649)." Furthermore, with respect to the assertion in the specification that any promoter can be used in the method (pages 13-17). NOTE: one of the promoters listed is considered inoperable by the prior art (Furlong, *supra*).

The court in Enzo 188 F.3d at 1374, 52 USPQ2d at 1138 states:

It is well settled that patent applications are not required to disclose every species encompassed by their claims, even in an unpredictable art. However, there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed.

In re Vaeck, 947 F.2d 48, 496 & n.23. 30 USPQ2d 1438, 1445 &n23 (Fed. Cir. 1991)(citation omitted). Here, however, the teachings set forth in the specification provide no more than a "plan" or "invitation" for those of skill in the art to experiment...; they do not provide sufficient guidance or specificity as to how to execute that plan. See Fiers v. Revel. 984 F.2d.1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993); In re Wright, 999 F.2d...[1557], 1562, 27 USPQ2d...[1510], 1514. [Footnote omitted].

On this record, it is apparent that the specification provides no more than a plan or invitation in view of the art of record exemplifying the unpredictability of using a genus of promoters to express the gene encoding PON1, for those skilled in the art to perform an undue amount of experiment with a genus of promoters so as to provide an expression cassette as intended by the as-filed specification at the time the invention was made.

See also Genentech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366, 42, USPQ2d 1001, 1005 (Fed. Cir. 1997)

("Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable the public to understand and carry out the invention.")

In view of the art of record and the lack of guidance provided by the specification; the specification does not provide reasonable detail for what promoters can be used in the claimed method and the art of record is does not provide what is lacking in the specification, and it would take one skilled in the art an undue amount of experimentation to reasonably extrapolate from the assertion in the specification to the full breadth of the claimed invention. Therefore, the as-filed specification is not fully enabled for the claimed invention.

Applicant's arguments, see pages 1-14, filed 11/17/06, with respect to 112 first paragraph enablement have been fully considered and are partially persuasive. Applicant's argument teaches that, at the time of filing, gene therapy was considered enabled. In addition, the working example in the specification reasonably correlates to the practicing the claimed method in a genus of cells or subjects. However, applicant did not address the unpredictability of using a genus of promoters to express the PON1 in a genus of cells. See Furlong (*supra*). Thus, it would require undue amount of experimentation to practice the full scope of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-5 and 9-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5 and 9-25 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps.

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See MPEP § 2172.01. The omitted steps are: exposing the cell or subject to an organophosphate toxin. The steps of claim do no complete the preamble of the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 9-15, and 17-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Hudson et al. (US 5,629,193). Hudson teaches gene transfer method for preventing cell death due to organophosphate poisoning comprising delivering a viral vector comprising a promoter operably linked to a nucleic acid encoding paraoxonase (PON) (columns 7-8) and In re Sasse, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). Hudson teaches that a number of viral vectors can be used (columns 4-5 and 12). Hudson teaches that there are two alleles of PON, now known as PON1 type R and PON 1 type Q (column 1). Hudson teaches that chlorpyrifos oxon is hydrolyzed by either allele product at the same or nearly same rate (column 1). Hudson teaches that the composition can be administered using any convenient manner (column 8).

NOTE: applicant argues that the evidence of record would overwhelmingly support the conclusion that one skilled in the art would find the present claims enabled (see pages 9 and 14 of applicant's arguments filed on 11/17/06).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hudson et al. (US 5,629,193) taken with Mackness et al. (Gen. Pharmac., 31, 329-336, 1998, cited on a PTO-1449). Hudson teaches gene transfer method for preventing cell death due to organophosphate poisoning comprising delivering a viral vector comprising a promoter operably

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linked to a nucleic acid encoding paraoxonase (PON) (columns 7-8) and In re Sasse, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). Hudson teaches that there are two alleles of PON, now known as PON1 type R and PON 1 type Q (column 1). Hudson teaches that chlorphyrifos oxon is hydrolyzed by either allele product at the same or nearly same rate (column 1). Hudson teaches that the composition can be administered using any convenient manner (column 8). However, Hudson does not specifically deliver the nucleic acid to a liver cell.

However, at the time the invention was made, Mackenss teaches that organophosphates are activated by a process in the liver (page 329).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Hudson taken with Mackness, namely to deliver the nucleic acid to a liver. One of ordinary skill in the art would have been motivated to combine the teaching to study the detoxification of an organophosphate in a liver cell.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Douglas Schultz, PhD, SPE – Art Unit 1635, can be reached at (571) 272-0763.

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Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Brian Whiteman

